II. REMARKS

Upon entry of the amendments, claims 10, 14 to 23, and 44 to 45 will be pending.

A. Regarding the Interview

The present invention is directed to screening assays for identifying compounds that can interfere with binding of a synaptic activation protein and metabotropic glutamate receptor (mGluR) as defined. As discussed in the Interview with the Examiner, the specification discloses various binding assays that were used to identify and characterize binding of a Homer synaptic activation protein and two mGluR proteins (mGluR1α and mGluR 5), and discloses that such assays can be used in screening assays.

More specifically, the specification discloses that a GST-Homer fusion protein was linked to an affinity column and used to bind mGluR expressed in HEK-293 cells (exogenous) and hippocampus (endogenous); following elution from the column, mGluR was detected using an anti-mGluR antibody and labeled second antibody (see page 12, lines 11-17; page 22, line 23, to page 23, line 14; and Figure 5). Similarly, the specification discloses that a two hybrid assay using Homer as the "bait" identified mGluR binding proteins from a rat brain cDNA library (see page 14, lines 9-13; page 14, line 29, to page 15, line 4; page 22, lines 1-10). The specification also discloses that an anti-Homer antibody bound to agarose beads co-immunoprecipitated Homer and mGluR (page 15, lines 15-23; page 23, lines 16-23; Figure 6; see, also, Figure 10E). Thus, the specification discloses various assays that detect binding of a Homer synaptic activation protein with an mGluR.

The specification further discloses that the polypeptides of the invention can be used in screening assays for identifying drugs that modulate the interaction of a synaptic activation protein and mGluR (page 18, lines 8-11), and that such screening assays can be performed using assay formats for measuring the protein-protein interaction (page 18, lines 15-17; see, also, page 3, line 27, to page 4, line 4). The specification also exemplifies a solid phase immunoassay for screening test compounds to identify a compound that interferes with binding of a synaptic

activation protein and mGluR (page 25, lines 1-9; see, also, page 18, lines 20-31). Thus, the specification discloses binding assays useful as the basis for screening assays to identify compounds that interfere with binding of a synaptic activation protein and mGluR, as claimed.

B. Information Disclosure Statement

An Information Disclosure Statement ("IDS") has not been filed in the instant application. This application is a Continuation of U.S. Application No. 09/042,428, filed March 13, 1998, now issued U.S. Patent No. 6,294,355. An IDS was filed in accordance with the provisions of 37 CFR §§ 1.97-98 in the above-referenced parent application. Therefore, Applicant respectfully submits the IDS filed in the parent case is "considered" pursuant to MPEP § 609(I)(2)(A). However, Applicant is submitting an IDS, Form PTO-1449 and a copy of the cited references concurrently herewith.

C. Regarding the Amendments

Claims 11 and 13 and pursuant to the restriction requirement, claims 1 to 9, 12, and 24 to 43 are canceled herein without disclaimer, and without prejudice to Applicants pursuing the subject matter encompassed within one or more of the claims in an application claiming the benefit of priority of the subject application.

Claim 10 has been amended to clarify that the claimed method provides a screening assay for identifying compounds that interfere with the binding of a synaptic activation protein having at least 70% identity to SEQ ID NO:2 and an mGluR comprising SEQ ID NO:10 or SEQ ID NO:11. The amendment is supported, for example, at page 18, lines 15-17, and by claim 11 as originally filed (see, also, page 16, line 32 to page 17, line 5).

Claim 10 also has been amended to more clearly set forth the steps of the claimed methods, i.e., "adding the test compound" to the reaction mixture, and "detecting a change in binding" in the presence as compared to the absence of the test compound. The amendment is

supported, for example, at page 3, lines 33-35; and page 18, lines 20-28, and, therefore, does not add new matter.

Claim 14, which previously depended from claim 13 (now cancelled), has been amended to depend from claim 10, which incorporates the language of previously pending claim 13, and to clarify that the mGluR is "mGluR5 or mGluR1α". As such, the amendments merely address formalities and do not add new matter.

Claim 15 has been amended to clarify that a synaptic activation protein useful in a screening assay of the invention can be a Homer protein comprising SEQ ID NO:2. The amendment clarifies that the previously recited term "having" was intended as "open language", allowing, for example, that the Homer protein comprise a fusion protein, for example, with GST. The amendment is supported, for example, at page 11, lines 28-31, which discloses cloning the Homer coding sequence into vectors that generate a GST-Homer fusion protein or LexA-Homer fusion protein (see, also, page 12, lines 14-16; page 14, lines 10-11).

Claim 18 has been amended to specify that the synaptic activation protein is a GST fusion protein. The amendment is supported, for example, at page 11, lines 28-31, and, therefore, does not add new matter.

Claim 19 has been amended to clarify that the claimed method is performed using a co-immunoprecipitation assay. The amendment is necessitated by the amendment of claim 10, which previously referred to a "means for detecting", to recite the active step of "detecting." As such, it is submitted that the amendment merely addresses a formality, and does not add new matter.

Claim 20 has been amended to clarify that the mGluR polypeptide comprises a "detectable label." The amendment is supported, for example, at page 18, lines 23-27, and, therefore, does not add new matter.

Claim 21 has been amended to clarify the steps for using a labeled antibody specific for an mGluR to detect a change in binding of a synaptic activation protein and mGluR. The amendment is supported, for example, at page 18, lines 23-25.

Claim 22 has been amended such that the language conforms to that of amended claim 20, from which claim 22 depends. As such, the amendment merely addresses a formality, and does not add new matter.

New claim 44 and 45 have been added. New claim 44 is supported, for example, at page 13, line 15, to page 15, line 5, and by Example 5 (page 22, lines 1-10). New claim 45 is supported, for example, at page 15, lines 12-14; and page 22, line 31, to page 23, line 5. As such, new claims 44 and 45 are supported by the specification.

It is submitted that the amended and new claims do not require a new search or consideration because they specifically address the issues set forth in the Office Action, or merely cancel claims or clarify the subject matter regarded as the invention. The amendments were not made earlier in prosecution because it was believed that the previous amendments addressed the outstanding grounds of rejection. The amendments do not add more claims (new claims 44 and 45) than were finally rejected (claims 11 and 13), and, it is submitted, place the claims in condition for allowance, or in better condition for appeal. As such, it is respectfully requested that the amendments be entered.

D. Regarding the Restriction Requirement

Pursuant to the Restriction Requirement, claims 1 to 9, 12, and 24 to 43 have been cancelled.

E. Regarding the Priority

It is stated in the Office Action that the relationship of the priority application to the subject application is not indicated. The Specification has been amended to indicate that the subject application is a Continuation of U.S. Application No. 09/042,428. As such, it is requested that this objection be withdrawn..

F. Rejections under 35 U.S.C. § 112

The rejection of claims 10, 11 and 13 to 23 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time the subject application was filed is respectfully traversed.

The claims are rejected as encompassing components other than synaptic activation proteins and cellular binding proteins as disclosed in the subject application. For example, it is stated that the claims are directed to the use of any cellular binding proteins, but that only mGluR proteins comprising an SSSL or SSTL sequence are disclosed in the specification as binding with a Homer synaptic activation protein. Claim 10 has been amended to clarify that the components of a screening assay of the invention include an isolated synaptic activation protein having at least 70% sequence identity to a polypeptide comprising SEQ ID NO: 2 (i.e., rat Homer), and an isolated mGluR comprising SSSL (SEQ ID NO: 10) or SSTL (SEQ ID NO: 11), wherein the synaptic activation protein binds to the mGluR in the absence of the test compound. The specification discloses such proteins and their ability to bind (see, for example, page 3, lines 6-19; page 16, line 29, to page 17, line 8), and that such proteins can be used in a screening assay (see page 3, line 27, to page 4, line 4). As such, it is submitted that claim 10 is supported by the subject application and, therefore, does not constitute new matter.

With respect to claim 18, it is stated that the application does not provide basis for a "GST pulldown" assay. The claims have been amended to correspond to the subject matter disclosed in the subject application. For example, claim 18 has been amended to clarify that a synaptic activation protein useful in the claimed method can be a fusion protein comprising GST, and new claim 45 recites that the fusion protein is linked to a solid support (see, for example, page 22, line 31, to page 23, line 5). As such, it is submitted that claim 18, and new claim 45, are supported by the subject application and, therefore, do not constitute new matter.

It is further stated in the Office action that the detection limits set forth in claims 18 and 19 are not supported by the specification because, while such detection methods are discussed in Examples 6 and 7 of the application, the Examples do not disclose adding a test

compound and selecting a compound in view of changed binding when compared to a control. As discussed in Section A, above, and in the Interview held February 17, 2004, the subject application broadly discloses the use of binding assays, including solid phase affinity assays, two hybrid assays, and co-immunoprecipitation assays. Further, the specification discloses that the polypeptide compositions have utility as components of screening assays for identifying drugs that can affect the interaction of the synaptic activation protein and mGluR (see, e.g., page 18, lines 8-29). As such, it is submitted that, when considered as a whole, the subject application clearly envisions that the various binding assays used to identify and characterize binding of a Homer synaptic activation protein with an mGluR would be useful in a screening assay as claimed.

With respect to the assay limitations for claims 16 and 20 to 23, it is stated that they are disclosed only with respect to mGluR5 or mGlur1α and PI-linked mGluR activity. As discussed above, claim 10 has been amended to more clearly define the synaptic activation protein and mGluR components useful in the screening assay. In view of the amendment, and based on the support discussed in Section A, above, it is submitted that the subject application supports the claimed subject matter.

In summary, the claims have been amended to more clearly define the components of the screening assay of the invention, and the specification discloses several assays that are well known in the art as useful for measuring protein-protein interactions, including disclosing that such assays are useful for detecting binding of a synaptic activation protein such as rat Homer (SEQ ID NO: 2) with an mGluR comprising an SSSL or SSTL sequence (e.g., mGluR1α and mGluR5), and have utility in assays to identify compounds that alter such binding. As such, it is submitted that the skilled artisan, reading the claims in view of the specification, would have known that Applicants' were in possession of the claimed screening methods at the time the subject application was filed. Accordingly, it is respectfully requested that the objection to the specification be withdrawn, and that the corresponding rejections of the claims under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description be removed.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to the subject application.

Please charge any additional fees, or made any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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